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79. (New) The isolated anti-TPBD antibody of claim 75, wherein said antibody has specific reactivity with SEQ ID NO:24.

80. (New) The isolated anti-TPBD antibody of claim 75, wherein said antibody has specific reactivity with SEQ ID NO:25.

AS
EL
81. (New) Antibody according to claim 75, wherein said antibody is a monoclonal antibody.

82. (New) A cell line producing the monoclonal antibody of claim 81.

83. (New) An antibody according to claim 75, wherein said antibody is a polyclonal antibody.--

REMARKS

Claims 1 to 73 are pending. Claims 1 to 7, 12 to 45 and 47 to 67 have been withdrawn from examination as directed to non-elected subject matter. Claims 8, 9, 11, 46 and 68 to 73 have been amended herein and new claims 74 to 83 have been added herein. Thus, upon entry of the present amendments, claims 8 to 11, 46, and 68 to 83 will be under examination.

Regarding the amendments

Claim 8 has been amended to independent form. The amendment to claim 8 is supported, for example, by claim 1 as originally filed.

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Claims 9 and 11 have been amended to depend from claims 8 or 74. The amendments to claims 9 and 11 are supported in the specification, for example, at page 50, lines 25-32.

Claim 46 has been amended to conform with the elected subject matter by reciting that the therapeutic composition contains an isolated anti-TPBD antibody having specific reactivity with TPBD amino acid sequence SEQ ID NOS:8, 12, 19, 20, 21, 22, 23, 24 or 25. The amendment to claim 46 is supported in the specification, for example, at page 12, lines 8-26.

Claim 68 has been amended to conform with the elected subject matter by reciting an isolated anti-TPBD antibody having specific reactivity with a TRAF protein binding site of TPBD amino acid sequence SEQ ID NOS:8, 12, 19, 20, 21, 22, 23, 24 or 25. The amendment to claim 68 is supported in the specification, for example, at page 12, lines 8-26.

Claim 69 has been amended to conform with the elected subject matter by reciting an isolated anti-TPBD antibody having specific reactivity with TPBD amino acid sequence SEQ ID NOS:8, 12, 19, 20, 21, 22, 23, 24 or 25.

Claims 70 to 73 have been amended to correct antecedent basis in view of the amendment to base claim 69. The amendments to claims 70 to 73 add no new matter.

New claim 74 depends from claim 8 and is directed to an isolated anti-TPBD antibody having specific reactivity with TPBD

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amino acid sequence SEQ ID NOS:20, 21 or 22. New claim 74 is supported in the specification, for example, at page 12, lines 8-26 and page 50, lines 20-23.

New claim 75 is directed to an isolated anti-TPBD antibody having specific reactivity with TPBD amino acid sequence SEQ ID NOS:8, 12, 23, 24 or 25. New claim 75 is supported in the specification, for example, at page 12, lines 8-26 and page 50, lines 20-23.

New claims 76 to 80 depend from claim 75 and are each directed to an isolated anti-TPBD having specific reactivity with one of the TPBD SEQ ID NOS recited in the Markush group of base claim 75. New claims 76 and 80 therefore add no new matter.

New claims 81 to 83 depend from claim 75, and are directed to a TPBD monoclonal antibody, cell-line producing a monoclonal antibody and TPBD polyclonal antibody. New claims 81 to 83 are supported in the specification, for example, at page 50, lines 28-32, and by claims 8 to 10 as originally filed.

As set forth above, the amendments and new claims are supported by the specification and claims as originally filed and do not add new matter. Accordingly, Applicants respectfully request that the Examiner enter the amendments and new claims.

Applicants have set forth above the amendments in clean form as required under 37 C.F.R. § 1.121 (c)(i). Attached as

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Appendix A is a marked up version of the amendments with the changes indicated with brackets and underlining as required under 37 C.F.R. § 1.121 (c)(ii).

Applicants acknowledge that method claims within the scope of the allowable product claims will be rejoined and examined at the time the product claims are indicated to be allowable.

Regarding the rejection under 35 U.S.C. § 112, second paragraph

The rejection of claims 68 to 73 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite is respectfully traversed.

The Office Action states that claims 68 and 69 are indefinite for reciting the term "effective agent." Specifically, the Office Action alleges that the claims recite an "effective agent" without defining how to measure an effective agent versus an ineffective agent. Applicant respectfully submits that the term "effective agent" is clear and definite in view of guidance in the specification for identifying an effective agent, for example, by the method set forth in original claim 37. Nevertheless, the rejection has been rendered moot by the amendment herein of claim 68 to conform with the elected subject matter of the present application by reciting an isolated anti-TPBD antibody. Accordingly, Applicants request removal of this rejection of claims 68 and 69 under 35 U.S.C. § 112, second paragraph.

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The Office Action states that claims 68, 72 and 73 are indefinite for reciting the phrase "association of TPBD with a TNF family receptor or a TRAF protein, TRAF protein or a TRAF-associated protein." Applicants respectfully point out that claim 68 does not recite the objected phrase. Applicants have amended claims 69, 72 and 73 to correct the obvious typographical error in the objected phrase by removing the duplication of the words "TRAF protein." Accordingly, Applicants request removal of the rejection of claims 68, 72 and 73 under 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. § 102(b)

The rejection of claims 8, 9, 46 and 68 under 35 U.S.C. § 102(b) as allegedly anticipated by Inoue (WO 97/38099) is respectfully traversed. Applicants respectfully submit that the isolated anti-TPBD antibodies of claims 8, 9 and 68, and therapeutic composition of claim 46, as amended, are novel over the cited reference.

Regarding claims 8 and 9, directed to isolated anti-TPBD antibodies having specific reactivity with TPBD SEQ ID NO:19, Applicants point out that WO 97/38099 describes monoclonal antibodies that bind TRAF5, rather than SEQ ID NO:19. The amino acid sequence of TRAF5 as reported in GenBank by Inoue, J., provided herewith as Exhibit 1, does not contain SEQ ID NO:19. Therefore, the antibody described in WO 97/38099 does not

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anticipate claim 8 or dependent claim 9. Accordingly, Applicants request removal of this rejection of claims 8 and 9 under 35 U.S.C. § 102(b).

Regarding claims 46 and 68, which have been amended herein to recite an isolated anti-TPBD antibody having specific reactivity with TPBD amino acid sequence SEQ ID NOS:8, 12, 19, 20, 21, 22, 23, 24 or 25, Applicants respectfully submit that the description in WO 97/38099 of an antibody that binds TRAF5 does not anticipate the claimed composition (claim 46) or anti-TPBD antibody (claim 68). In this regard, the amino acid sequence of TRAF5 is distinct from all of the TPBD SEQ ID NOS recited in claims 46 and 68. Therefore, the TRAF5 antibody described in WO 97/38099 does not anticipate the claimed therapeutic composition or isolated anti-TPBD antibody. Accordingly, Applicants request removal of this rejection of claims 46 and 68 under 35 U.S.C. § 102(b).

The rejection of claims 8, 11 and 68 under 35 U.S.C. § 102(b) as allegedly anticipated by Nagai et al., FEBS Letters, 418:23-26 (1997), is respectfully traversed. Applicants respectfully submit that the isolated anti-TPBD antibodies of claims 8, 11, and 68, as amended, are novel over the cited reference.

Regarding claims 8 and 11, directed to isolated anti-TPBD antibodies having specific reactivity with TPBD SEQ ID NO:19, Applicants point out that Nagai et al. describes polyclonal antibodies that bind to the carboxyl terminus of SPOP

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(amino acids 186-374), rather than to a region of SPOP that contains the TRAF domain encompassed by SEQ ID NO:19. Specifically, whereas the claimed isolated anti-TPBD antibodies are specifically reactive with a sequence within amino acids 1-164 of SPOP, the polyclonal antibodies described in Nagai et al. have no reactivity with amino acids 1-185 of SPOP (page 25, Figure 5A). Submitted herewith as Exhibit 2 is the amino acid sequence of SPOP, which has been highlighted to show the locations of the TRAF domain encompassed by SEQ ID NO:19 and the binding region of the Nagai et al. polyclonal antibody. As is apparent, there is no overlap between the region of SPOP containing SEQ ID NO:19 and the region bound by the polyclonal antibodies described in Nagai et al. Therefore, Nagai et al. does not anticipate the claimed isolated anti-TPBD antibodies. Accordingly, Applicants request removal of this rejection of claims 8 and 11 under 35 U.S.C. § 102(b).

As amended, claim 68 recites a therapeutic composition containing an isolated anti-TPBD antibody having specific reactivity with TPBD amino acid sequence SEQ ID NOS:8, 12, 19, 20, 21, 22, 23, 24 or 25. Whereas Nagai et al. describes polyclonal antibodies that bind to the carboxyl terminus of SPOP (amino acids 186-374), none of Applicants' claimed anti-TPBD antibodies have specific reactivity with this region of SPOP. Rather, the claimed anti-TPBD antibodies have specific reactivity with the TRAF domain of SPOP, located in the amino terminus of SPOP (SEQ ID NO:24); with proteins different from SPOP, such as HAUSP (SEQ ID NOS:8 and 23) and TRAF-7 (SEQ ID NOS:12 and 25); or with the TRAF domain of SPOP and highly related TPBDs having

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specific consensus amino acid sequences not present within the carboxy terminus of SPOP (SEQ ID NOS:19, 20, 21 and 22). For this reason, Nagai et al. does not anticipate the therapeutic composition of claim 68. Accordingly, Applicants request removal of this rejection of claim 68 under 35 U.S.C. § 102(b).

The rejection of claims 68, 69, 71 and 72 under 35 U.S.C. § 102(b) as allegedly anticipated by Rothe et al., Proc. Natl. Acad. Sci. USA, 93:8241-8246 (1996), is respectfully traversed. Applicants respectfully submit that the isolated anti-TPBD antibodies of claims 68, 69, 71 and 72, as amended, are novel over the cited reference. In this regard, claims 68, 69, 71 and 72 recite antibodies that have specific reactivity with TPBD polypeptides (SEQ ID NOS:8 and 12); TRAF domains of TPBD polypeptides (SEQ ID NOS:23, 24 and 25); and consensus TRAF domains of TPBD polypeptides (SEQ ID NOS:19 to 22). In contrast, Rothe et al. does not describe antibodies specifically reactive with SEQ ID NOS:8, 12, 19, 20, 21, 22, 23, 24 or 25. Accordingly, Applicants respectfully request removal of this rejection under 35 U.S.C. § 102(b).

The rejection of claims 68, 69 and 73 under 35 U.S.C. § 102(b) as allegedly anticipated by MacLachlan et al. Journal of Cellular Biochemistry 71:467-478 (1998), is respectfully traversed. Applicants respectfully submit that the isolated anti-TPBD antibodies of claims 68, 69, and 73, as amended, are novel over the cited reference. Claims 68, 69, and 73 recite antibodies specifically reactive with SEQ ID NOS:8, 12,

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19, 20, 21, 22, 23, 24 or 25. In contrast, MacLachlan et al. does not describe an antibody that binds to a TPBD having SEQ ID NOS:8, 12, 19, 20, 21, 22, 23, 24 or 25. As such, claims 68, 69 and 73 are novel over MacLachlan et al. and Applicants request removal of this rejection under 35 U.S.C. § 102(b).

Rejection under 35 U.S.C. § 103(a)

The rejection of claims 8, 9, 10 and 68 under 35 U.S.C. § 103(a) as allegedly obvious over Lelias et al. (US 5,705,615) in view of Young et al. (US 6,346,605), is respectfully traversed. Applicants respectfully point out that the correct citations for US 5,705,615 and US 6,346,605 appear to be Lim et al. and Lee et al., respectively, rather than Lelias et al. and Young et al.

Applicants respectfully submit that the isolated anti-TPBD antibodies of claims 8, 9, 10 and 68, as amended, are non-obvious over the cited combination of references. US 5,705,615 describes an antibody that binds to Ht_{m4} and inhibits binding of Ht_{m4} to TRAF-1, TRAF-2, TRAF-3 and KAP (column 12, lines 56-64); US 6,346,605 describes TRAF-2 binding to TNFR. Neither of these references teach or suggest an antibody that binds to SPOP (SEQ ID NO:24), HAUSP (SEQ ID NOS:8 and 23), TRAF-7 (SEQ ID NOS:12 and 25) or closely related sequences having a common motif not contained in TRAF-1, TRAF-2, TRAF-3 or KAP (SEQ ID NO:19, 20, 21 and 22). Without some teaching or suggestion of an antibody having specific reactivity with the

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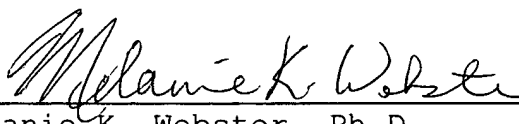
recited sequences, the cited patents cannot render obvious the claimed isolated anti-TPBD antibodies.

CONCLUSION

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, she is invited to call the undersigned agent or Cathryn Campbell.

Respectfully submitted,

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